



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,532	07/13/2001	Napoleone Ferrara	10466/50	2313

35489 7590 08/01/2005

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER

DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
----------	--------------

1647

DATE MAILED: 08/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/904,532

Applicant(s)

FERRARA ET AL.

Examiner

Regina M. DeBerry

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 June 2005.
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-47 and 49-51 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 39-47, 50 and 51 is/are rejected.
7) ☒ Claim(s) 49 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 13 July 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/06/05
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 January 2005 has been entered.

Status of Application, Amendments and/or Claims

Claims 39-47, 49-51 are under examination.

Information Disclosure Statement

The information disclosure statement(s) (IDS) filed 06 December 2004 and 19 January 2005 (duplicate) were received and comply with the provisions of 37 CFR §§1.97 and 1.98. They have been placed in the application file and the information referred to therein has been considered as to the merits.

Specification

The disclosure is objected to because of the following informalities: The phrase "Table 7 (cont.)" appears inappropriately in the middle of pages 219-221.

Art Unit: 1647

The disclosure contains blank spaces and/or pages (pages 65, 90, 94-98).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-43, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence and a specific activity. The subject matter sought to be patented as defined by the claims is not supported by an enabling disclosure because the specification has failed to teach one skilled in the art which changes in the polypeptide to make that will preserve the structure and function. Absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for proteins, that even a single amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases.

Art Unit: 1647

The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding enablement. Please see Wells (1990, Biochemistry 29:8509-8517).

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions. Applicant has provided no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Undue experimentation is a conclusion reached by weighing all of the Wands Factors. If one skilled in the art can readily anticipate the effect, than there is predictability in the art. In this case, however, the art is unpredictable based on the evidence provided. Furthermore, the instant polypeptide is novel and does not share significant sequence identity with any known polypeptide or polypeptide family. Thus, the prior art lacks detailed information about active sites, domains, etc. Without

Art Unit: 1647

sufficient guidance, the changes which can be made in the structure and still maintain sufficient activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and screen same for inhibition of endothelial cell growth activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 39-43, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification provides adequate written description for SEQ ID NO:127, but not variants.

The claims are drawn to polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence and a specific activity. The instant specification contemplates but does not exemplify variants of the protein wherein

Art Unit: 1647

the variant can have any number of substitutions, deletions, insertions and/or additions in SEQ ID NO:127, wherein said variants inhibit endothelial cell growth. The specification does not provide any guidance as to what changes should be made and which regions of the instant protein are functionally and structurally critical. There is no description of variants of SEQ ID NO:127 that exist, while still maintaining function (inhibition of endothelial cell growth). The instant protein is novel and does not share significant sequence identity with any known polypeptide or polypeptide family. There is not even identification of any particular portion of the structure that must be conserved.

The disclosure fails to describe the common attributes or characteristics that identify the members of the genus. The genus is highly variant because a significant number of structural differences between genus members are permitted. Thus, SEQ ID NO:127 alone is insufficient to describe the genus. The disclosure fails to provide a representative number of species to describe the genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or

Art Unit: 1647

simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:127, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39 and 44 are indefinite because of the recitation, "An isolated polypeptide". It is not clear if the instant polypeptide reads on a fragment or a full-length

Art Unit: 1647

polypeptide. Amending the claims to recite, "The isolated polypeptide", would be remedial.

Claims 39-47 are indefinite because of the recitation, "the amino acid sequence of the polypeptide shown in Figure 46 (SEQ ID NO:127)". Amending to claims to recite, "the amino acid sequence of SEQ ID NO:127", would be remedial.

Claims 39-43 are indefinite because of the recitation, "wherein said polypeptide inhibits endothelial cell growth" (claim 39) and "wherein said polypeptide inhibits VEGF stimulation of endothelial cell growth" (claims 40-43). The metes and bounds of the instant claims cannot be determine because it is unclear what the difference is between the polypeptide of claim 39 and the polypeptide of claims 40-43. Applicant is asked to specifically point in the specification, the patentable distinction between the claims and/or amend the claims accordingly.

Lastly, claim 44 is indefinite because it is drawn to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:127 that lacks a biological activity. The metes and bounds of the instant claim cannot be determine because it unclear what the difference is between the polypeptide of claim 44 and the polypeptide of claims 39-43. Applicant is asked to specifically point in the specification, the patentable distinction between the claims and/or amend the claims accordingly.

Claim Objections

Claim 49 is objected to because it depends from a rejected claim.

Art Unit: 1647

Conclusion

Claims 39-47, 50 and 51 are rejected.

Claim 49 is objected to.

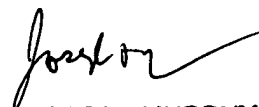
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



RMD
7/22/05



JOSEPH MURPHY
PATENT EXAMINER